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WENDEROTH, LIND & PONACK, L.L.P.
1030 15th Street, N.W.,
Suite 400 East
Washington, DC 20005-1503

EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ddalecki@wenderoth.com
eoa@wenderoth.com

Office Action Summary	Application No.	Applicant(s)	
	10/566,502	NAKASHIMA ET AL.	
	Examiner	Art Unit	
	Isis A. Ghali	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1,4-9,11 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-9,11 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/19/2010, 08/25/2010, 08/30/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The receipt is acknowledged of applicants' amendment and IDS filed 07/19/2010, IDS filed 08/25/2010 and IDS filed 08/30/2010.

Claims 1, 4-9, 11 and 13 are pending and included in the prosecution.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 4-9, 11 and 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Amendment made to the claims to recite that 4-(2-methyl- 1-imidazolyl)- l 2,2-diphenylbutylamide or a medically acceptable salt thereof **"as the sole active ingredient"** introduces new matter that was not described in the original specification. Applicant refers to page 10 line 1 of the present specification for support, however, recourse to the specification, and pages 9 and 10 in particular, applicant disclosed "The preparation according to (7) above, containing as an

active ingredient a dissolved form of 4-(2-methyl-l- imidazolyl)-2,2-diphenylbutylamide alone". This paragraph refers to the presence of dissolved form of the active agent alone. This is evident and supported by the following paragraph in lines 2-4 of page 10 of the specification that states: "The preparation according to (7) above, containing as active ingredients dissolved and non-dissolved forms of 4-(2- methyl-l-imidazolyl)-2,2-diphenylbutylamide". Therefore, when applicant disclosed sole active agent, it was the dissolved active agent, rather than the other alternative of the combination of dissolved and non-dissolved active agent. If applicant contends there is support for this limitation, then applicant is requested to specify the page and line of said support. In accordance to MPEP 714.02, applicant should specifically point out to where in the disclosure a support for any amendment made to the claims can be found.

It has been held that "Any negative limitation or exclusionary proviso must have basis in the original disclosure." See In re Johnson, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977). In *In re Johnson*, the court noted that any negative limitation or exclusionary proviso *must have basis in the original disclosure. Only* if alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. Note that a lack of literal basis in the specification for a negative limitation may not be sufficient to establish a prima facie case for lack of descriptive support. *Ex parte Parks*, 30 USPQ2d 1234, 1236 (Bd. Pat. App. & Inter. 1993). See MPEP § 2163 - § 2163.07(b) for a discussion of the written description requirement of 35 U.S.C. 112, first paragraph.

In the present case the negative limitation/exclusionary proviso does not have basis in the original disclosure, and the alternative elements were not positively recited in the specification. See also *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983), aff'd mem., 738 F.2d 453 (Fed. Cir. 1984). Any claim containing a negative limitation, which does not have basis in the original disclosure, should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement. In *Purdue Pharma LP v Faulding, Inc., 230 F.3d 1320, 1326, 56 USPQ2d 1481, 1486 (Fed. Cir. 2000)*, the court noted that with respect to *In re Ruschig, 371 F.2d 990, 154 USPQ 118 (CCPA 1967)*, "*Ruschig* makes clear that one cannot disclose a forest in the original application, and then later pick out a tree of the forest and say, "here is my invention". In order to satisfy the written description requirement, the blaze marks directing the skilled artisan to that tree must be in the originally filed disclosure." *Purdue* is relevant in this case, because the Applicants disclosed a genus ("a forest") in the original application, then later picked out two specific compounds ("a tree of the forest"), and are now saying, "here is my invention". In order to satisfy the written description requirement, according to *Purdue*, the Applicants must disclose the specific compounds in the originally filed disclosure." (See (56 USPQ2D 1481). More from *Purdue*: The case of *In re Ruschig*, 379 F.2d 990, 154 USPQ 118 (CCPA 1967), is instructive here (see page 1487). The claim at issue in that case was directed to a single compound. The appellants argued that, although the compound itself was not disclosed, one skilled in the art would find support for the claimed compound in the general disclosure of the genus of compounds to which the claimed compound belonged. The *Ruschig* court

rejected that argument, stating: [i]t is an old custom in the woods to mark trails by making blaze marks on the trees. It is of no help in finding a trail or in finding one's way through the woods where the trails have disappeared-or have not yet been made, which is more like the case here-to be confronted simply by a large number of unmarked trees. We are looking for blaze marks, which single out particular trees. We see none. *Id.* at 994-95, 154 USPQ at 122.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1, 4-9, 11 and 13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20 of copending Application No. 11/815,499. Although the conflicting claims are not identical,

they are not patentably distinct from each other because the subject matter claimed in the instant application is fully disclosed in the referenced copending applications and would be covered by any patent granted on the copending applications since the referenced copending applications and the instant application are claiming common subject matter as follows: transdermal preparation containing 4-(2-methyl-l-imidazoolyl)-2,2-diphenylbutylamide. The present claims and the co-pending claims are obvious over each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

5. Applicant's arguments filed 07/19/2010 have been fully considered but they are not persuasive. Applicants argue that the object of the invention of serial No. 11/815,499 is different from that of the present invention, and the essential features of Serial No. 11/815,499 are distinguished from those of the present invention as evident by claims 19 and 20 that require specific limitations.

In response to this argument, it is argued that claims of the copending application are more limited and represent a species of the genus currently claimed by the present application, and species anticipates genus. All the elements of the present claims are claimed by the copending application and would be covered by any patent granted on the copending applications.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1, 4-9, and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over the article by Miyachi et al. ("Synthesis and Antimuscarinic Activity of a Series of 4-(1-Imidazolyl)-2,2-diphenylbutyramides: Discovery of Potent and Subtype-selective Antimuscarinic Agents", IDS filed 01/31/2006), in view of the article by Nitti ("Transdermal Therapy for Overactive Bladder: Present and Future", IDS filed 12/10/2008) and further in view of either Versi et al. (US 2003/0191172, currently listed on PTO 892) or Landau et al. (US 6,846,823, currently listed on PTO 892).

Applicant Claims

Claim 1 is directed to a transdermal preparation containing 4-(2-methyl-1-imidazolyl)-2,2-diphenylbutylamide or a medically acceptable salt thereof as the sole active ingredient, and an external preparation base.

Determination of the Scope and Content of the Prior Art

(MPEP §2141.01)

Miyachi teaches that the inhibitory action of 4-(2-methyl-1-imidazolyl)-2,2-diphenylbutylamide (KRP-197) on bladder contractions is 15-19 times more potent than oxybutynin and with a similar duration of action (p 1157, col.1, ¶ 2). KRP-197 is fivefold more selective for bladder than oxybutynin (p 1157, col.2, ¶ 2). Thus, KRP-197 could have therapeutic potential for the treatment of symptoms in diseases associated with altered smooth muscle contractility and tone with a lower incidence of side effects

(paragraph bridging page 1157 and 1158). Therefore, Miyachi implies the use of KRP-197 alone as an alternative to oxybutynin, and not with it.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Miyachi however is silent regarding dosage forms and routes of administration of KRP-197.

Nitti teaches that transdermal delivery of certain pharmacologic agents that treat overactive bladder offers distinct advantages including the ability to bypass the gastrointestinal environment, fewer side effects, and increased bioavailability (page 531). Further, administration of anticholinergic drugs transdermally demonstrated a significant reduction in the anticholinergic side effects that often lead to frustration and treatment discontinuation (page 533, col.3, ¶ 1). Nitti concludes that the studies that compare oral with transdermal overactive bladder medications with respect to patient satisfaction and preference may help promote more widespread use of transdermal drug delivery as first line therapy for overactive bladder (page 536, col.1 and 2).

Versi teaches treating of varieties of incontinence-related conditions using antimuscarinic agents including KRP-197 (abstract; paragraphs 0010, 0016; table 2; claim 27). The active agents can be administered by means of transdermal patch using conventional technology in order to reduce side effects and obtain improved subject compliance (paragraph 0070). Transdermal patches may contain adhesive reservoir containing the drug dissolved and/or dispersed in the adhesive (paragraph 0080). The

teaching of Versi of dissolved and/or dispersed drug in the reservoir meets the limitation of claim 9 that drug is dissolved and non-dissolved.

Landau teaches treating at least one symptoms of lower urinary tract disorder including urinary frequency, urgency, incontinence, nocturia and enuresis using composition comprising antimuscarinic including KRP-197 (abstract; col.18, lines 38-43; col.20, line 18). The composition can be transdermal composition delivered from patch that provides controlled release of the drug through the skin for long period from one application (col.38, lines 40-42, 50-55). Transdermal patch comprises laminate structure comprising backing layer, release liner, and reservoir containing the drugs and permeation enhancer (col.45, lines 5-43).

Adhesive taught by Versi and Landau and permeation enhancer taught by Landau read on the claimed external preparation means because according to applicants' disclosure on page 15, lines 1-7, "external preparation base" can be amphipathic solubilizing agent, a suspension base, a softener, an emulsifier, a buffer, a transdermal permeability enhancer, a tackifier, a tackiness enhancer, an adhesive, a skin irritancy mitigator, and an additive.

Finding of Prima Facie Obviousness Rational and Motivation

(MPEP §2142-2143)

At the time of the invention it was known that KRP-197 is antimuscarinic drug that is more potent than other antimuscarinic drugs known as this time such as oxybutynin as taught by Miyachi. At the time of the invention Nitti preferred transdermal

delivery of drugs that treat overactive bladder and suggested more widespread use of transdermal drug delivery as first line therapy for overactive bladder. It was further known at the time of the invention that KRP-197 can be delivered in transdermal devices as taught by both of Versi and Landau.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention treat overactive bladder using KRP-197 as an alternative to oxybutynin as taught by Miyachi and deliver the drug transdermally as taught by Nitti, Versi and Landau. One would have been motivated to do so because Nitti teaches that transdermal delivery of pharmacologic agents that treat overactive bladder offers distinct advantages including the ability to bypass the gastrointestinal environment, fewer side effects, and increased bioavailability, and further, administration of anticholinergic drugs transdermally demonstrated a significant reduction in the anticholinergic side effects that often lead to frustration and treatment discontinuation and suggests more widespread use of transdermal drug delivery as first line therapy for overactive bladder. One would further be motivated to deliver KRP-197 utilizing transdermal device because both of Versi and Landau teaches that KRP-197 can be delivered from transdermal devices that provides reduced side effects, improved patient compliance and controlled release of the drug. One would reasonably expect formulating transdermal device comprising KRP-197 as the sole active agent to treat overactive bladder that delivers the drug in a controlled manner to treat urinary bladder disorders effectively with minimal undesired side effects and improved patient compliance.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

10. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Miyachi et al. in view Nitti and either Versi et al. or Landau et al. as applied to claims 1, 4-9 and 11, and further in view of Luo et al. (US 6,586,000, currently listed on PTO 892).

Applicant Claims

Claim 13 is further recite the structure of the transdermal device comprising a reservoir, comprising a mixture of 4-(2-methyl-l-imidazolyl)-2,2-diphenylbutylamide and a single or combination of the external preparation bases; and a structural body comprising a membrane for controlling drug permeation, an adhesive layer, a support, and a peelable liner.

Determination of the Scope and Content of the Prior Art

(MPEP §2141.01)

The combined teaching of Miyachi, Nitti, and either one of Versi or Landau are discussed above. The combination of the references teaches transdermal device comprising KRP-197, and Landau further teaches transdermal device comprising reservoir, backing layer and peelable release liner.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

The references however, do not teach the structure of the transdermal device to comprise a membrane to control the release of the drug and the adhesive layer as claimed by claim 13.

Luo teaches transdermal device comprising reservoir containing active agent, adhesive, and further permeation enhancer. The device comprises backing layer, release liner, skin contact adhesive and rate controlling membrane to control the rate at which the drug permeates out of the device (col.4, lines 17-33; col.25, lines 41-43; col.26, lines 10-15). The skin contact adhesive maintains the device in transmitting relationship to the body surface (col.4, lines 27-30).

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention treat overactive bladder using KRP-197 delivered from transdermal device comprising reservoir containing the drug, backing layer and peelable release liner as taught by the combination of Miyachi, Nitti, Versi and Landau and further add a rate controlling membrane and skin contact adhesive to the device as taught by Luo. One would have been motivated to do so because Luo teaches the rate controlling membrane controls the rate at which the drug permeates out of the device and the skin

contact adhesive layer maintains the device in transmitting relationship to the body surface. One would reasonably expect formulating transdermal device comprising KRP-197 in an adhesive reservoir having backing layer and peelable release liner and further has rate controlling membrane and skin contact adhesive layer wherein the device deliver the drug to the skin in a controlled manner while being secured to the skin of the user.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

11. Applicant's arguments filed 07/19/2010 have been fully considered but they are not persuasive.

Applicants argue that Miyachi does not suggest a transdermal preparation like those of the present invention. The production of pharmaceutical products in the form of transdermal preparations are achieved not only based on the level of the active ingredient, but such production can be significantly varied by the stability of the compound in external patches, the permeability of the compound through skin, the irritancy of the preparation, and the like. In other words, even if the activity of KRP-197 is larger than oxybutynin, it is uncertain whether the compound is effectively utilized in transdermal preparations as pharmaceutical drugs.

In response to this argument, applicants attention is directed to the scope of the present claims that are directed to product, and all the elements of the product are taught by the combined teachings of the prior art. At the time of the invention it was known that KRP-197 is antimuscarinic drug that is more potent than other antimuscarinic drugs known as this time such as oxybutynin as taught by Miyachi. At the time of the invention Nitti preferred transdermal delivery of drugs that treat overactive bladder and suggested more widespread use of transdermal drug delivery as first line therapy for overactive bladder. It was further known at the time of the invention that KRP-197 can be delivered in transdermal devices as taught by both of Versi and Landau.

It is further argued that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir.1986). In the instant case, Miyachi teaches the claimed compound for the same uses, and further teaches the compound as superior to the other compounds and drugs used for the same purpose. Versi and Landau teach that such a compound can be included in transdermal devices to provide systemic delivery of such a compound. Nitti further teaches the advantage of transdermal delivery over oral delivery. The present invention as a whole is taught and obvious over the combined teachings of the cited prior art.

Applicants argue that Versi teaches administering a cyclooxygenase inhibitor alone or in combination with an anticholinergic drug. Landau teaches administering a compound that has 5-HT3 receptor antagonist activity and Nnoradrenaline reuptake Inhibitor (NARI) activity, and an anticholinergic drug may be co-administered. Both Versi and Landau list KRP-197 as one example of known anticholinergic drugs and they do not suggest whether KRP-197 contained in transdermal preparations is actually effective. The simple disclosure as one exemplary anticholinergic drug would not motivate one skilled in the art to use it in a transdermal preparation. Versi and Landau, taken with Miyachi, do not disclose or suggest the transdermal preparation including KRP-197 as the sole active ingredient, as instantly claimed.

In response to this argument, it is argued that the effectiveness of KRP-197 already taught by Miyachi, and Versi and Landau are relied upon for the solely teaching of suitability of administering KRP-197 from transdermal devices. At the time of the invention it was known that KRP-197 is antimuscarinic drug that is more potent than other antimuscarinic drugs known as this time such as oxybutynin as taught by Miyachi. At the time of the invention Nitti preferred transdermal delivery of drugs that treat overactive bladder and suggested more widespread use of transdermal drug delivery as first line therapy for overactive bladder. It was further known at the time of the invention that KRP-197 can be delivered in transdermal devices as taught by both of Versi and Landau. Therefore, all the elements of the present invention were known at the time of the invention.

In considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972).

Regarding the limitation of "sole active ingredient", it is further noted that the present claims' language "containing" does not exclude other active agent in the transdermal device. In re *Mannesmann Demag Corp. v. Engineered Metal Products Co.*, 793 F.2d 1279, 230 USPQ 45 (Fed. Cir. 1986), and *In re Crish*, 393 F.3d 1253, 73 USPQ2d 1364 (Fed. Cir. 2004), the court stated that the use of "consists" in the body of the claims did not limit the open-ended "comprising" language in the claims (emphases added). Id. At 1257, 73 USPQ2d at 1367. The court affirmed the Board's interpretation that the transition phrase "consists" did not limit the claims to only the recited members, and that "the transition language comprising" allowed the claims to cover other members. This applies here on the present claims that have the open-ended language "containing" in the permeable that allows the claims to cover other active ingredients,

and because the expression "sole active agent" falls within the body of the claims following the open-ended expression.

Applicants argue that Nitti discusses transdermal therapy as compared to oral therapy for overactive bladder, but considering the deficiencies of the other references as discussed above, if Nitti were combined with these other references, the result would still not suggest the presently claimed invention.

In response to this argument, it is argue d that Nitti, as applicants admit, is relied upon for the teaching that transdermal delivery of pharmacologic agents that treat overactive bladder offers distinct advantages including the ability to bypass the gastrointestinal environment, fewer side effects, and increased bioavailability, and further, administration of anticholinergic drugs transdermally demonstrated a significant reduction in the anticholinergic side effects that often lead to frustration and treatment discontinuation and suggests more widespread use of transdermal drug delivery as first line therapy for overactive bladder. The present invention as a whole is taught by the combination of the cited prior art.

Applicants argue that claim 13 is indirectly dependent on claim 1, which is patentable over the other references for the reasons discussed above, it is apparent that even if the references were combined in the manner suggested by the Examiner, the result would still not suggest the subject matter of claim 13.

In response to this argument, it is argued that the subject matter of claim 1 is obvious over the combination of Miyachi, Nitti, Versi or Landau. Luo is relied upon for the solely teaching of the conventional structure of transdermal devices.

Finally, it has been held that "When a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious." *KSR Int 'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007) (quoting *Sakraida v. AG Pro, Inc.,* 425 U.S. 273,282 (1976)). "When the question is whether a patent claiming the combination of elements of prior art is obvious," the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions. In addition, "To determine whether there was an apparent reason to combine the known elements in the way a patent claims, it will often be necessary to look to interrelated teachings of multiple patents; to the effects of demands known to the design community or present in the marketplace; and to the background knowledge possessed by a person having ordinary skill in the art. To facilitate review, this analysis should be made explicit. But it need not seek out precise teachings directed to the challenged claim's specific subject matter, for a court can consider the inferences and creative steps a person of ordinary skill in the art would employ". Pp. 11-14. KSR INTERNATIONAL CO. v. TELEFLEXINC. ET AL. (2007). A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one

versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969).

In the light of the foregoing discussion, the Examiner's ultimate legal conclusion is that the subject matter as a whole as defined by the claims would have been obvious within the meaning of 35 U.S.C. 103 (a).

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis A. Ghali whose telephone number is (571) 272-

0595. The examiner can normally be reached on Monday-Thursday, 6:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571) 272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Isis A Ghali/
Primary Examiner, Art Unit 1611

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